NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

TAKEDA PHARMACEUTICAL COMPANY LIMITED et al., Plaintiffs, v. NORWICH PHARMACEUTICALS, INC. et al., Defendant.	**Civil Action No. 20-8966 (SRC)** **OPINION & ORDER**

CHESLER, District Judge

This matter comes before the Court on the application for claim construction by Plaintiffs Takeda Pharmaceutical Company Limited and Takeda Pharmaceuticals U.S.A. Inc. (collectively, "Takeda") and Defendant Norwich Pharmaceuticals, Inc. ("Norwich.") This case arises from Hatch-Waxman litigation regarding patents related to the pharmaceutical Vyvanse®. Norwich is a pharmaceutical company which has filed ANDA No. 214547 to produce generic versions of the Vyvanse® products. Takeda owns the eighteen U.S. patents-in-suit, and has asserted 412 claims against Norwich in this litigation. The patents are: U.S. Patent Nos. 7,105,486 ("the '486 patent"), 7,223,735 ("the '735 patent"), 7,655,630 ("the '630 patent"), 7,659,253 ("the '253 patent"), No. 7,659,254 ("the '254 patent"), 7,662,787 ("the '787 patent"), 7,662,788 ("the '788 patent"), 7,671,030 ("the '030 patent"), 7,671,031 ("the '031 patent"), 7,674,774 ("the '774 patent"), 7,678,770 ("the '770 patent"), 7,678,771 ("the '771 patent"), 7,687,466 ("the '466

patent"), 7,687,467 ("the '467 patent"), 7,700,561 ("the '561 patent"), 7,713,936 ("the '936 patent"), 7,718,619 ("the '619 patent"), and 7,723,305 ("the '305 patent") (collectively, "the patents-in-suit"). These patents generally relate to compositions and methods of treatment comprising L-lysine-d-amphetamine ("LDX") compounds. The parties seek claim construction of terms in these eighteen patents.

ANALYSIS

I. The law of claim construction

A court's determination "of patent infringement requires a two-step process: first, the court determines the meaning of the disputed claim terms, then the accused device is compared to the claims as construed to determine infringement." Acumed LLC v. Stryker Corp., 483 F.3d 800, 804 (Fed. Cir. 2007). "[W]hen the district court reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history), the judge's determination will amount solely to a determination of law." Teva Pharms. USA, Inc. v. Sandoz, Inc., 135 S. Ct. 831, 841 (2015).

The focus of claim construction is the claim language itself:

> It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude. Attending this principle, a claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to 'particularly point[] out and distinctly claim[] the subject matter which the patentee regards as his invention.'

Innova/Pure Water, Inc. v. Safari Water Filtration Sys., 381 F.3d 1111, 1115-1116 (Fed. Cir. 2004) (citations omitted).

The Federal Circuit has established this framework for the construction of claim language:

> We have frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.' We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application. The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation. . .
>
> In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean. Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.

Phillips v. AWH Corp., 415 F.3d 1303, 1312-1314 (Fed. Cir. 2005) (citations omitted).

II. Claim construction of the disputed terms

A. Term 1: the mesylate salt of LDX

The parties dispute the meaning of three terms which relate to the mesylate salt of LDX: "L-lysine-d-amphetamine mesylate," "mesylate salt of L-lysine-d-amphetamine," and "… wherein said salt is a mesylate salt." These terms appear in 51 claims of fifteen patents in issue. Plaintiffs propose this construction: "a salt of L-lysine-d-amphetamine containing at least one CH3SO3- anion, which can be obtained from methanesulfonic acid." Defendant proposes this construction: "'mesylate' / 'a mesylate salt' means 'a salt with any number of mesylate ions associated with it."

The briefs focus this dispute on one central question: what ratios of mesylate to LDX ions do salts of LDX encompass? For example, the parties agree that LDX dimesylate means "a salt of L-lysine-d-amphetamine containing two CH_3SO_3- anions;" in that example, the ratio of mesylate ions to LDX ions is 2:1. A complication arises from the fact that Plaintiffs' position has shifted over time, and they now offer two related alternative constructions. In the Joint Claim Construction Statement, Plaintiffs proposed the construction already stated, that LDX mesylate salts must have at least one mesylate ion for each LDX ion, and thus that the ratio in question must be 1:1 or greater. While Plaintiffs' briefs have continued to assert this, Plaintiffs' briefs also assert a second, narrower construction: LDX mesylate salts must have at least one, but not more than two, mesylate ions (i.e., the range of ratios is 1:1 through 2:1 only.) (See, e.g., Pls.' Br. at 7.) Defendant proposes that LDX mesylate salts may have any number of mesylate ions for each LDX ion, and thus that, as long as both elements of the ratio in question are greater than zero, a compound falls within the scope of LDX mesylate salts. Thus, Defendant contends that, for example, a compound with a ratio of 1:3, with one mesylate ion and three LDX ions, would fall within the scope of these terms; under Plaintiffs' construction, it would not.

Plaintiffs begin their argument with the intrinsic evidence but, in short, Plaintiffs do not cite any intrinsic evidence that sheds light on the issues in dispute.[1] Defendant goes right to the extrinsic evidence, which Plaintiffs also rely on. The real issues here are issues of underlying fact about what a pharmaceutical chemist would have understood about the structure of mesylate salts of LDX at the time of the invention. Plaintiffs' narrower construction relies on the factual

[1] In brief, the intrinsic evidence tells us that there is a genus of mesylate salts of LDX, and that one species in that genus is the dimesylate salt of LDX. These are not matters in dispute.

proposition that a POSA would understand LDX mesylate salts to include only LDX monomesylate and LDX dimesylate, whereas Defendant's construction relies on the factual proposition that a POSA would understand that a mesylate salt of LDX may have any non-zero number of mesylate ions, including compounds with more LDX ions than mesylate ions. The parties' dispute about claim language thus turns on a subsidiary factual dispute about what a POSA would understand about what ratios for LDX mesylate salts are possible. In largest part, this is a battle of the experts, a battle which Plaintiffs clearly win.

To support its proposed construction, Defendant relies on the declarations of its expert, Dr. Hollingsworth. In his opening declaration, Dr. Hollingsworth discusses claim 3 of the '030 patent, and opines: "a POSA would also understand that claim 3 encompasses L-lysine-d-amphetamine mesylate salts that have ratios of mesylate ions to L-lysine-d-amphetamine that are less than 1:1." (Hollingsworth Dec. ¶ 48.) Dr. Hollingsworth proceeds to opine that LDX mesylate salts could have ratios of 1:2, 3:2, 1:4, and 1:3. (Id. at ¶ 52.) In support, Dr. Hollingsworth points to published research on chlorhexidine phosphanilate and tromethamine salt which, he contends, have ratios less than 1:1. (Id. at ¶ 53.) In his responsive declaration, Dr. Hollingsworth also cites a patent that, he contends, discloses a hemimesylate salt of a drug, indoximod; the hemimesylate salt has a ratio of .5:1.[2] (Hollingsworth Resp. Dec. ¶ 11, 13.)

In sum, Defendant relies on three pieces of extrinsic evidence: 1) the opinion of Dr. Hollingsworth that LDX mesylate salts are possible which have ratios of 1:2, 3:2, 1:4, and 1:3

[2] Plaintiffs argue that, based on the date of publication, this reference is not in the prior art, and dispute the matter of whether it discloses a true hemimesylate salt. (Pls.' Reply Br. 1-3.)

(hereinafter, the "Disputed Mesylate Salts"); 2) publications disclosing that salts not containing LDX or mesylate exist with a ratio less than 1:1; and 3) a publication, dated May 17, 2018, that Defendant contends discloses a hemimesylate salt. Neither Defendant nor Dr. Hollingsworth points to any intrinsic evidence that meaningfully supports Defendant's position.

Plaintiffs challenge Dr. Hollingsworth's declarations on several grounds. First, Plaintiffs note that three of four of the chemical diagrams of the Disputed Mesylate Salts that Dr. Hollingsworth had in his original declaration contained errors, which Dr. Hollingsworth conceded. (Hollingsworth Dep. 101:4-9.) Second, Plaintiffs point out that Dr. Hollingsworth does not meet his own criteria for a POSA (Hollingsworth Dec. ¶ 23), as he lacks two years of experience in drug discovery and formulation, which Dr. Hollingsworth admitted (Hollingsworth Dep. 46:4-16.) Third, Plaintiffs contend that the Disputed Mesylate Salts are not, in fact, salts, as that term is generally understood in the chemical arts, relying on the declaration of their expert, Dr. Chyall. Instead, Plaintiffs contend, Dr. Hollingsworth's corrected diagrams of the Disputed Mesylate Salts depict co-crystals or mixtures, comprising combinations of true mesylate salt forms of LDX as well as neutral LDX molecules. Plaintiffs argue that salts cannot contain neutral molecules.

In support of their assertion that salts cannot contain neutral molecules, Plaintiffs first point out that Defendant's opening brief provides this definition: "A salt of L-lysine-d-amphetamine contains two components: (1) an L-lysine-d-amphetamine ion and (2) its counterion, such as mesylate." (Defs.' Br. 26.) Plaintiffs agree with this definition and point out that it does not include neutral molecules. Plaintiffs also offer the opinion of Dr. Chyall that Dr. Hollingsworth's corrected diagrams of the Disputed Mesylate Salts depict co-crystals or

mixtures, comprising both true mesylate salt forms of LDX as well as neutral LDX molecules. (Chyall Resp. Dec. ¶¶ 111, 114, 115.) Dr. Chyall stated that these mixtures contain both true salt forms (either LDX monomesylate or LDX dimesylate) as well as neutral LDX freebase; they are not pure salts with the claimed ratios. (Chyall Resp. Dec. ¶ 115-119.) Dr. Chyall explained that the components of salts are bonded by only ionic bonds, and that the Disputed Mesylate Salts are mixtures containing some ionic bonds and some non-ionic hydrogen bonds. (Id.) Because of this, Dr. Chyall concluded that the Disputed Mesylate Salts are not true salts with ratios below 1:1.

The parties point to no intrinsic evidence of record which resolves this dispute of underlying scientific fact; it must be decided based on the extrinsic evidence, the opinions of the experts. This Court finds that Dr. Chyall's opinion is more persuasive and that he is more credible as an expert.

As to the credibility of the experts, Plaintiffs make several persuasive points. Although Defendant claims that Dr. Hollingsworth is "an expert in pharmaceutical salts" (Defs.' Br. 13), Dr. Hollingsworth admitted that he did not have experience in salt selection for any pharmaceutical company. (Hollingsworth Dep. 47:20-48:9.) As already stated, Plaintiffs point out that Dr. Hollingsworth does not meet his own criteria for a POSA, lacking two years of experience in drug discovery and formulation.[3] Dr. Chyall stated that he had worked in the areas of salt selection for pharmaceutical products as well as drug formulation; Defendant did not

[3] After the Federal Circuit decided Kyocera Senco Indus. Tools, Inc. v. ITC, 2022 U.S. App. LEXIS 1739, at *11 (Fed. Cir. Jan. 21, 2022), Plaintiffs wrote to advise the Court of the decision, which states: "To offer expert testimony from the perspective of a skilled artisan in a patent case—like for claim construction, validity, or infringement—a witness must at least have ordinary skill in the art."

dispute this. Dr. Hollingsworth conceded that several of his original chemical diagrams contained errors. The Court finds that Dr. Chyall is more credible as an expert witness.

This Court also finds Dr. Chyall's critique of Dr. Hollingsworth's opinions about the Disputed Mesylate Salts to be persuasive. The Court credits Dr. Chyall's opinion that the molecules comprising salts are bound by ionic bonds only, and that the Disputed Mesylate Salts contain some non-ionic bonds. The parties do not dispute that salts contain only ions and counterions, with no neutral particles. The Court credits Dr. Chyall's opinion that the Disputed Mesylate Salts include neutral particles and therefore are not compounds comprised only of LDX mesylate salts. Having weighed the extrinsic evidence, the Court concludes that, at the time of the invention, a POSA would not understand LDX mesylate salts to include the Disputed Mesylate Salts.

As noted, Plaintiffs submitted an opening brief which formally proposes one construction but then argues in favor of both that construction as well as a narrower one. Plaintiffs formally propose: "a salt of L-lysine-d-amphetamine containing at least one CH3SO3- anion, which can be obtained from methanesulfonic acid." The brief argues for this construction, as well as this narrower one:

> A POSA would further understand that a mesylate salt of L-lysine-d-amphetamine must have at least one, but not more than two, mesylate (or CH3SO3-) anions associated with it. (Chyall ¶¶ 32-36, 43-52). Because L-lysine-d-amphetamine can have two sites on the molecule that can accept protons from acids to form salts, a POSA would expect that only these two sites are available for protonation. (Chyall ¶¶ 33-36, 47).

(Pls.' Br. 7.) This is a potent argument and, this Court finds, Plaintiffs' best argument about how a POSA would understand LDX mesylate salts. Neither party has pointed to anything that supports the proposition that a POSA would expect a mesylate salt of LDX to have more than 2

mesylate ions bound to one LDX ion. Dr. Chyall pointed out the two possible binding sites on the chemical diagram of LDX that Norwich used in its FDA filings: "a POSA would understand that L-lysine-d-amphetamine can theoretically accept a CH_3SO_3- anion at either or both of the protonated amine groups (-NH_3^+) on the L-lysine-d-amphetamine molecule." (Chyall Dec. ¶ 47.) Dr. Chyall further stated:

> L-lysine-d-amphetamine has only two basic sites and therefore can accept a maximum of two protons regardless of the excess of acid used to protonate the molecule. Scientists may use excess acid to drive salt-formation reactions to completion, but ultimately the number of basic sites present on the molecule determines the allowable stoichiometries of the resulting salts.

(Chyall Resp. Dec. ¶ 134.) This Court finds Dr. Chyall to be persuasive and credits Plaintiffs' argument that POSA would understand that a mesylate salt of LDX contains at least one, but not more than two, mesylate ions.

In Teva, the Supreme Court articulated the principles a Court must apply when a claim construction decision requires the Court to make subsidiary factual findings. The Court stated:

> In some cases, however, the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period. In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the "evidentiary underpinnings" of claim construction that we discussed in *Markman.*

Teva Pharm. USA, Inc. v. Sandoz, Inc., 574 U.S. 318, 331-32 (2015) (citation omitted.) This Court credits Dr. Chyall's statements and makes a subsidiary factual finding that that a mesylate salt of LDX contains at least one, but not more than two, mesylate ions. This is the understanding that a POSA would have had, at the time of the invention, about mesylate salts of LDX.

Once the subsidiary factual finding has been made, the Supreme Court stated, the facts as determined must be applied to the legal issue of claim construction:

> [I]f a district court resolves a dispute between experts and makes a factual finding that, in general, a certain term of art had a particular meaning to a person of ordinary skill in the art at the time of the invention, the district court must then conduct a legal analysis: whether a skilled artisan would ascribe that same meaning to that term in the context of the specific patent claim under review.

Id. at 332. Here, the parties do not dispute that the POSA would have based the understanding of the claim terms at issue on the understanding of the subsidiary factual question, that the meaning of "mesylate salt of LDX" turns on the POSA's understanding of the underlying chemistry. This Court therefore determines, as a matter of law, that a POSA would have ascribed that same meaning to the term "mesylate salt of LDX" in the claims at issue. Based on this analysis, this Court adopts Plaintiffs' narrower proposed construction of "mesylate salt of LDX." As a result, this Court revises Plaintiffs' proposed construction accordingly: "a mesylate salt of LDX" means "a salt of L-lysine-d-amphetamine containing at least one, but not more than two, CH_3SO_3- anions, which can be obtained from methanesulfonic acid."

B. Term 4: "limited bioavailability of amphetamine when administered through alternative routes of administration"

This term appears in claims 1 and 18 of the '735 patent; those claims are quite similar. Claim 1 is representative:

> 1. A pharmaceutical composition comprising an unprotected prodrug and one or more pharmaceutically acceptable additives;
>
> wherein said prodrug consists of L-lysine-d-amphetamine or a pharmaceutically acceptable salt thereof;
>
> wherein said composition is in a form suitable for oral administration;
>
> wherein said composition provides release of amphetamine as an active from said

> prodrug following oral administration;
>
> and wherein said prodrug has **limited bioavailability of amphetamine when administered through alternative routes of administration.**

Defendant contends that this phrase has its ordinary meaning, but offers no interpretation of what that ordinary meaning is. Plaintiffs propose this construction: "lower extent of absorption of the amphetamine released following administration of L-lysine-d-amphetamine or a salt thereof through parenteral[4] routes of administration often employed in illicit use compared to the extent of absorption of d-amphetamine following administration of a comparable molar dose of d-amphetamine or a salt thereof through parenteral routes of administration often employed in illicit use."

Plaintiffs' proposed construction raises two principal issues, both about understanding the meaning of "limited" bioavailability in this term. Plaintiffs contend that "limited bioavailability:" 1) means "lower extent of absorption of amphetamine" 2) in the context of a comparison of parenteral administration of LDX (or a salt) to parenteral administration of d-amphetamine (or a salt) (hereinafter, the "Comparator Issue.")

Defendant opposes Plaintiffs' position with a trenchant observation:

> excluding the terms for which there are agreed constructions and that are separately briefed, the only remaining words in [Term 4] are "limited," "of," "when," and "through."

(Defs.' Br. 21.) Defendant thus reminds Plaintiffs that the focus of claim construction is the words in the claims themselves: the Court construes particular words. Inasmuch as Plaintiffs have not asserted arguments about the meaning of "of," "when," or "through," the only word left

[4] "Parenteral" administration here means other than oral administration, i.e., snorting, injecting, smoking.

to construe is "limited." What does "limited" mean here?

Plaintiffs' proposed construction attempts to pack a lot of meaning into one word, "limited." On the one hand, Plaintiffs contend that "limited" here not only means "lower," but they also sweep in the Comparator Issue. As to the Comparator Issue, Plaintiffs appear to propose a method for "establishing" the limited bioavailability:[5] 1) administer, by a parenteral route, LDX or a salt thereof, and then measure the absorption of the amphetamine it releases; 2) administer, by a parenteral route, a comparable molar dose of d-amphetamine or a salt thereof, and then measure the absorption of the d-amphetamine it releases; and then 3) compare the value of the first step to the value of the second step to determine whether the first step value is lower.

In support of their proposed construction, Plaintiffs rely on a number of examples in the specification, particularly Examples 11 and 12. No example in the specification uses the phrase "limited bioavailability" except for Example 24, which Plaintiffs do not discuss. Example 11 bears this subheading: "Decreased Intranasal Bioavailability of L-lysine-d-amphetamine vs. Amphetamine." '735 patent, col.27 ll.23-24. Example 11 states this concluding sentence:

> Example 11 illustrates that when lysine is conjugated to the active agent d-amphetamine the bioavailability by the intranasal route is substantially decreased thereby diminishing the ability to abuse the drug by this route.

'735 patent, col.28 ll.20-23. Example 12 bears this subheading: "Intravenous Bioavailability of

[5] The Court wonders: did the patentees really draft claims for a pharmaceutical composition so as to include limitations pertaining to methods of demonstrating claimed properties? Plaintiffs' brief does not address this. Why should the methods used in Examples 11 and 12 get incorporated into the claims as limitations? For example, Dr. Taft opines: "A POSA would understand that the proper comparison for purposes of establishing the claims' limited bioavailability, is between the d-amphetamine as released from the prodrug and d-amphetamine itself." (Taft Dec. ¶ 41.) For the sake of discussion, even if this Court considers that correct, on what legal basis would this Court transform this opinion into a claim limitation? What does this have to do with the construction of the word, "limited"?

Amphetamine vs. L-lysine-d-amphetamine." '735 patent, col.28 ll.27-28. Example 12 states this concluding sentence:

> Example 12 illustrates that when lysine is conjugated to the active agent amphetamine the bioavailability of amphetamine by the intravenous route is substantially decreased, thereby diminishing the ability to abuse the drug by this route.

'735 patent, col.28 ll.49-53.

Although Examples 11 and 12 do not contain the word "limited," they both expressly deal with the bioavailability of amphetamine when LDX is administered by the intranasal and intravenous routes, two routes of parenteral administration. Furthermore, in both examples, the patentees describe the very low amount of d-amphetamine released into circulation from the LDX element; the patent's description of Figures 12 and 13 states that plasma concentrations of d-amphetamine have been compared, and this appears to be the basis for statements about decreased bioavailability from the administration of LDX.

Plaintiffs argue: "In these Examples, L-lysine-d-amphetamine has a lower extent of absorption of the amphetamine released following administration . . ." (Pls.' Br. 11.) While this is a correct use of the word, "lower," the word choice was made by Plaintiffs, not the patentees. No reasonable reader could agree that "lower" bioavailability completely and accurately describes the findings of Examples 11 and 12. In Example 11, the patent states that LDX "did not release any significant amount of d-amphetamine into circulation" and "the bioavailability by the intranasal route is substantially decreased thereby diminishing the ability to abuse the drug." '735 patent, col.28 ll.2-3,20-23. In Example 12, the patent states that LDX "did not release a significant amount of d-amphetamine" and "the bioavailability of amphetamine by the intravenous route is substantially decreased, thereby diminishing the ability

to abuse the drug." '735 patent, col.28 ll.33,50-53. These examples do not support construing "limited bioavailability" as "lower" in extent, relative to unconjugated d-amphetamine administered by the same route. Both examples describe the bioavailability as "substantially decreased," which does not have the same meaning as the word, "lower." Construing "limited" as "lower" would allow an unjustified expansion of claim scope.

It must be highlighted that this Court does not agree with Plaintiffs that one can determine the meaning of "limited bioavailability" in claims 1 and 18 by looking to two examples, among the many provided in the patent, neither of which even use the word, "limited." The Court observes only that the examples chosen by Plaintiffs not only do not support their construction of "limited" as "lower," but suggest that "lower" would substantially broaden the scope of the claims beyond what these examples support. Since this Court finds that Plaintiffs have not persuasively construed the term, "limited bioavailability," it need not reach those parts of Plaintiffs' arguments that concern the implied Comparator Issue.

Defendant, however, proposes no particular construction for Term 4, despite the requirement of L. Pat. R. 4.2(a) that parties propose constructions "for which 'plain and ordinary' meaning is asserted." Defendant asks the Court to adopt a construction which it has failed to propose.

The Federal Circuit has recognized a general rule, with two specific exceptions, to the construction of claim language:

> Claim terms are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history. We have recognized only two exceptions to this general rule: 1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution.

Unwired Planet, LLC v. Apple Inc., 829 F.3d 1353, 1358 (Fed. Cir. 2016) (citations omitted). Thus, as a general rule, there are three options for deriving meaning: 1) a claim term has its ordinary meaning as understood by the skilled artisan; 2) a patentee, acting as his or her own lexicographer, gives a claim term a special meaning; or 3) the Court infers a narrowed meaning based on a disavowal of scope in the specification or prosecution.

For this claim term, neither party has argued a theory of meaning premised on lexicography or disclaimer. Defendant expressly argues that the term has its ordinary meaning. Plaintiffs apply no label to their theory of construction, but rely on the general rule of Phillips that the specification "is the single best guide to the meaning of a disputed term." Phillips, 415 F.3d at 1315. Because the parties have not argued otherwise, and because the "words of a claim are generally given their ordinary and customary meaning," Wasica Fin. GmbH v. Cont'l Auto. Sys., 853 F.3d 1272, 1279 (Fed. Cir. 2017), the Court concludes that it is undisputed that, as to Term 4, the instant case presents no exception to the general rule, and Term 4 has its ordinary meaning.

The parties must further brief the question of the ordinary meaning of Term 4, keeping in mind that "a claim construction analysis must begin and remain centered on the claim language itself."[6] Innova, 381 F.3d at 1116. The parties shall consult and propose a briefing schedule

[6] The Court notes that claim 18 refers to "limited release of amphetamine" as well as "limited bioavailability of amphetamine." Perhaps considering both uses of the word, "limited," can help shed light on how the POSA would understand "limited bioavailability." The specification of the '735 patent has much to say on the subject of the "limiting" functionality of the invention, which the parties did not discuss in their briefs, such as:

> Without wishing to be limited to the following theory, we believe that overdose protection results from a natural gating mechanism at the site of hydrolysis that

for supplementary briefing on this question.

Similarly, as to Term 6, "C_{max} which results in euphoria," the parties have agreed that the phrase has its ordinary meaning, but Defendant has not proposed a particular construction, despite the requirement of L. Pat. R. 4.2(a) that it do so. Defendant shall submit a supplementary brief which proposes a particular construction of this term.

C. Term 9: "Amphetamine"

This dispute concerns the word "amphetamine," as used in over 60 claims across twelve patents. Plaintiffs propose that "amphetamine" should be construed differently, depending on the context, proposing eight different constructions for eight different contexts. In short, Plaintiffs propose that, sometimes, "amphetamine" should be construed as the genus of amphetamines, and sometimes, "amphetamine" should be construed as limited to d-amphetamine. Plaintiffs make a number of arguments in support.

Defendant proposes that "amphetamine" means "any sympathomimetic phenethylamine derivative that has central nervous system stimulant activity." Defendant asserts – and Plaintiffs do not dispute – that the '735 and '486 patents state this definition in their specifications, and that the remaining patents-in-issue incorporate by reference the '735 and '486 patents. Thus, Defendant argues, "amphetamine" should be construed as expressly defined in the specification.

Plaintiffs, in response, while admitting that the specifications of the '735 and '486 do

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> limits the release of the active amphetamine from the prodrug at greater than therapeutically prescribed amounts. Therefore, abuse resistance is provided by limiting the "rush" or "high" available from the active amphetamine released by the prodrug and limiting the effectiveness of alternative routes of administration.

'735 patent, col.9 ll.7-15.

contain the sentence, "'amphetamine' shall mean any sympathomimetic phenethylamine derivative that has central nervous system stimulant activity," insist that this is not a definition and should not constrain the construction of the terms at issue. Plaintiffs aptly cite the relevant Federal Circuit law: "To act as a lexicographer, a patentee must clearly set forth a definition of the disputed claim term and clearly express an intent to define the term." Pacing Techs., LLC v. Garmin Int'l, Inc., 778 F.3d 1021, 1024 (Fed. Cir. 2015). Those requirements are met here: the patentees clearly set forth a definition of "amphetamine" and clearly expressed an intent to define the term. In the '735 and '486 patents, the same definition of amphetamine appears in a part of the specification that defines quite a few other important claim terms; it is unambiguous that, there, the patentees defined various key terms. They read like definitions and this Court concludes that the patentees clearly stated a definition of "amphetamine" which controls the construction of the term.[7] Plaintiffs have not come close to providing any justification for overriding the express definition stated by the patentees.

"Amphetamine" means "any sympathomimetic phenethylamine derivative that has central nervous system stimulant activity."

D. Term 14: "isolated"

The claim term in dispute, "isolated," appears in the first two claims of the '787 patent:

> 1. A compound selected from the group consisting of **isolated** L-lysine-d-amphetamine and a pharmaceutically acceptable salt of L-lysine-d-amphetamine.
> 2. **Isolated** L-lysine-d-amphetamine.

[7] As this Court concluded when it considered very similar arguments in previous litigation over an overlapping group of LDX patents, "Defendants' proposed construction fits the express definition [in the specification], and this Court adopts Defendants' proposed construction of 'amphetamine.'" Shire LLC v. Amneal Pharms., LLC, 2013 WL 4045622, at *9 (D.N.J. Aug. 8, 2013).

Plaintiffs contend that, in these claims, "isolated" means "a substance separated from a crude mixture of reactants and/or solvents." Defendant proposes that it means "non-salt form."

Defendant first argues that its proposed construction prevents the phrase in claim 1, "pharmaceutically acceptable salt of L-lysine-d-amphetamine," from being superfluous. Defendant provides no support for this contention, nor does it explain how Plaintiffs' proposed construction renders that phrase superfluous.

Defendant then sensibly looks to how "isolated" is used in the specification, where it appears once only, in Example 2, which presents a description of a method for the synthesis of LDX, and states, in part:

> The crude product was dissolved in ethyl acetate and loaded on to a flash column (7 cm wide, filled to 24 cm with silica) and eluted with ethyl acetate. The product was **isolated**; the solvent reduced by rotary evaporation and the purified protected amide was dried by high-vac to obtain a white solid.

'787 patent, col.20 l.64-col.21 l.2. Defendant observes that this does not describe salt formation, and that, where the specification describes salt formation, the word "isolated" is not used, arguing that these facts support its proposed construction. This is unpersuasive; Defendant has pointed to no basis to believe that its interpretation of "isolated" makes any sense in the context of Example 2. While Defendant cites the statements of its expert, Dr. Hollingsworth, about "isolated" in Example 2, Dr. Hollingsworth says nothing to support the idea that the quoted section of Example 2 describes a step in which a salt form was transformed into a non-salt form. In fact, Dr. Hollingsworth offers only a circular interpretation: "In view of these disclosures, a POSA would understand that 'isolated' L-lysine d-amphetamine means that the L-lysine d-amphetamine molecule itself is isolated from other molecules and atoms, including those that form salts with L-lysine d-amphetamine." (Hollingsworth Dec. ¶ 61.)

There is no disagreement that "isolated" in the context of this patent generally means isolated from other molecules and atoms, and Dr. Hollingsworth provides no basis to understand this step in Example 2 as transforming a salt form of LDX into a non-salt form.

Together with one other meritless argument, this covers Defendant's case in support of construing "isolated" as "non-salt form." The Court finds Defendant has no support for its position.

Plaintiffs begin their argument with the use of "isolated" in Example 2, quoted above. Plaintiffs point to Dr. Chyall's opinion about "isolated" in the context of Example 2: "A POSA would understand that the term 'isolated' in the specification of the '787 patent refers to the separation of the product from a crude mixture using chromatography." (Chyall Dec. ¶ 55.) Dr. Chyall opines that this reading is consistent with Plaintiffs' construction, since the isolation in Example 2 appears to indicate a step in a synthesis process whereby chromatography is used to separate an intermediate product from a mixture of elements. (Id.) Indeed, Plaintiffs' proposed construction makes sense in the context of Example 2, whereas Defendant's proposed construction does not.

Plaintiffs also point to the use of "isolated" in seven references cited as prior art in the '787 patent. "[A]rt cited in the prosecution history of the patent constitutes intrinsic evidence." Arthrex, Inc. v. Smith & Nephew, Inc., 935 F.3d 1319, 1330 (Fed. Cir. 2019). Plaintiffs point to seven examples from these references in which, Plaintiffs argue, "isolated" is used consistently with their proposed construction.

In response, Defendant argues that the cited articles do not use "isolated" in the same context as in the claims at issue. Defendant cites no authority for the proposition that the

context must be identical. Rather, the Federal Circuit has stated:

> [W]hen prior art that sheds light on the meaning of a term is cited by the patentee, it can have particular value as a guide to the proper construction of the term, because it may indicate not only the meaning of the term to persons skilled in the art, but also that the patentee intended to adopt that meaning.

Kumar v. Ovonic Battery Co., 351 F.3d 1364, 1368 (Fed. Cir. 2003) (quoting Arthur A. Collins, Inc. v. Northern Telecom Ltd., 216 F.3d 1042, 1045 (Fed. Cir. 2000)). Kumar speaks of the prior art having "particular value as a *guide* to the proper construction," and the facts of Kumar shed light on this. At issue in that case was the meaning of the word "amorphous" in the claim phrase, "amorphous rare earth-transition metal alloy material." Id. at 1366. The prior art Polk patent contained an express definition of the term, "solid amorphous metal." This phrase was not identical to the claim term at issue, but the Kumar Court concluded that the definition stated in the Polk patent reflected the definition that would have been understood by the POSA, and held that the "Polk patent definition should control unless the specification clearly states an alternative meaning or this meaning was disclaimed during prosecution." Id. at 1368. Federal Circuit law does not require a strict identity of context between the claim term and the use in the prior art reference.

In the instant case, one prior art reference, international patent application WO 99/39691, contains Example 8, disclosing a method of synthesis of a compound of interest, which states, in relevant part: "The product was isolated by filtration, washed with IMS 2 x 12m1 and dried in vacuo at 40 to 45°C to yield the title compound . . ." (Roper Dec. Ex. 24 at TAKVYV01715276.) Dr. Chyall opined that this example, as well as the citations in the six other prior art references, shows a use of "isolated" that is consistent with Plaintiffs' construction. (Chyall Dec. ¶ 63.)

In opposition, Defendant cites Dr. Hollingsworth's statements, which only repeat the point that the contexts of use in the prior art references are not identical to the context in the claims at issue. (Hollingsworth Resp. Dec. ¶ 25.) Defendant also cites Dr. Chyall's deposition statements that a number of the prior art references do not involve LDX or salt forms. (Chyall Dep. 50-60.)

Nonetheless, as Plaintiffs point out in their responsive brief, Example 8 in WO 99/39691 refers to a salt form being isolated and thus appears to contradict Defendant's position. The title of Example 8 states: "Preparation of (1S 4R)-cis-. . .-methanol hemisulfate salt." (Roper Dec. Ex. 24 at TAKVYV01715276.) Thus, the cited statement in Example 8 states that, after being isolated by filtration, washed and dried, a hemisulfate salt resulted. Under Defendant's proposed construction of "isolated," "a non-salt form," how can a salt result from the product being isolated? The use of "isolated" in Example 8 in WO 99/39691 is contrary to Defendant's proposed construction. Under Federal Circuit law, this is intrinsic evidence that supports Plaintiffs' construction and contradicts Defendant's.

Plaintiffs argue as well that the prosecution history supports their construction, but this is uninformative, a dead end. In brief, during prosecution, the applicant originally submitted '787 claims 1 and 6 without the word "isolated." (Amended Claims dated May 7, 2007.) The examiner rejected these claims as obvious over the NL '901 reference, which disclosed LDX in a form protected by a tosyl group; the examiner stated that the removal of the tosyl group was a matter of "routine optimization" for a POSA. (Office Action dated November 12, 2008.) The record clearly shows that the insertion of "isolated" was an "examiner's amendment," discussed, and approved by the applicant, during a telephone interview held on either July 28, 2009 or

August 18, 2009. (Examiner's Amendment dated September 22, 2009.) The Notice of Allowance issued on September 22, 2009 identifies the insertion of "isolated" as an examiner's amendment agreed to by the applicant, and states reasons for the allowance of the claims. The reason provided by the examiner is that unprotected LDX is an intermediate created during the synthesis of the protected tosylated LDX, and that it was unexpected that this intermediate form would have utility/enablement for therapeutic use. In response, the applicants filed comments which disagreed with the examiner's statement, saying that NL '901 does not disclose the synthesis of either the protected or unprotected form of LDX, and that there was no evidence of record that either was an intermediate of the other. (Comments on Statement of Reasons for Allowance dated October 1, 2009.) The '787 patent subsequently issued as amended.

The documents in the file wrapper shed no light on how the applicants understood the word "isolated" in the Examiner's Amendment. Nor do the examiner's statements about reasons for allowance of the claims with the "isolated" amendment make clear how the examiner understood "isolated," setting aside the question of what use this Court could make of such statements. Dr. Chyall speculates: "The word 'isolated' seems to have been suggested by the Examiner to avoid covering L-lysine-d-amphetamine that might be formed in a hypothetical reaction scheme . . ." (Chyall Dec. ¶ 58.) Dr. Chyall observes, however, that the applicants filed a letter disagreeing with the examiner on this point, but agreed to the 'isolated' amendment. (Chyall Dec. ¶ 59.) It is not at all clear from this record what the applicants understood about the meaning of "isolated." The prosecution history does not help shed light on this question.

Defendant has failed to persuade this Court that there is any evidence to support its proposed construction. The intrinsic evidence supports Plaintiffs' proposed construction:

"isolated" means "a substance separated from a crude mixture of reactants and/or solvents."

E. Terms 16-20: the milligram terms

The parties raise two disputes here: 1) when a claim states a specific numerical dosage range, e.g., 25 mg to 50 mg, how precisely is that delimited? and 2) when a claim uses the word "about" in stating a specific numerical dosage range, e.g., about 25 mg to about 50 mg, what are the exact limits to that range? How much variation does "about" allow?

As to the first question, the parties agree that the milligram terms have their ordinary meaning, but disagree on what that meaning is. In short, Plaintiffs propose that there is some variability allowed, while Defendant proposes that the milligram numbers provide precise limits. Plaintiffs contend that it is well-understood in the art that manufacturing processes produce a small amount of variation, citing Dr. Chyall's statements that Defendant's ANDA provides for such minor variation in the dosage amounts.[8] While Defendant professes to disagree, its responsive brief concedes that the parties' experts, in fact, essentially agree: the claim terms stating a numerical range of whole numbers allow rounding to the nearest whole number. Defendant's expert, Dr. Barzman, testified at his deposition:

> Q. What level of precision is required by the term precisely?
>
> A. The precision required would be being rounded to the study dose. For example, 25 would be precise if it's rounded to 25.

[8] Dr. Chyall points to the "Uniformity of Dosage Units" statements in the ANDA, which refer to the USP 905 Content Uniformity standard. (See, e.g., Chyall Dec. ¶ 74, citing Roper Dec. Ex. 49 at NPILDX_000002747.) The Court takes judicial notice that United States Pharmacopeia (USP) publishes its standards online, and that USP 905, titled "Uniformity of Dosage Units," states, in relevant part: "To ensure the consistency of dosage units, each unit in a batch should have a drug substance content within a narrow range around the label claim." https://www.usp.org/sites/default/files/usp/document/harmonization/gen-method/q0304_stage_6_monograph_25_feb_2011.pdf (last visited March 3, 2022.)

> Q. So is it your opinion that precisely requires a variability of plus or minus .4 milligrams?
>
> A. Yes.

(Mathias Resp. Dec. Ex. 4 at 112:17-25.) Dr. Barzman expressly agreed that the level of precision required allowed ordinary rounding to whole numbers. Plaintiffs' responsive brief states: "Dr. Barzman now appears to largely agree with Dr. Chyall's definition." (Pls.' Resp. Br. 30.)

The Court finds that the parties have resolved their dispute about the degree of precision required by the milligram terms: the terms have their ordinary meaning, which allows for rounding to the nearest whole number.

As to the second milligram question, regarding claims 2-4 in the '561 patent, which refer to "about" a number of milligrams, the parties again agree that the terms have their ordinary meaning, but Defendant adds that the ordinary meaning of "about" is "approximately." Defendant cites the Federal Circuit's careful examination of this issue in Merck & Co. v. Teva Pharm. USA, Inc., 395 F.3d 1364, 1372 (Fed. Cir. 2005), which concluded: "We thus hold that the term 'about' should be given its ordinary and accepted meaning of 'approximately.'" See also Ferring B.V. v. Watson Labs, Inc., 764 F.3d 1382, 1389 (Fed. Cir. 2014) (same, citing Merck). Plaintiffs make no objection to construing "about" to mean "approximately." Given that Plaintiffs agree that "about" has its ordinary meaning in the claims at issue, the Court construes "about" in the claims at issue to have its ordinary meaning of "approximately."

In conclusion, the Court construes the terms at issue as follows. "A mesylate salt of LDX" means "a salt of L-lysine-d-amphetamine containing at least one, but not more than two, CH_3SO_3- anions, which can be obtained from methanesulfonic acid." Term 4, "limited," has its

ordinary meaning, which will be determined in a second phase of claim construction. "C_{max} which results in euphoria" has its ordinary meaning, which will be determined in a second phase of claim construction. "Amphetamine" means "any sympathomimetic phenethylamine derivative that has central nervous system stimulant activity." "Isolated" in the claims at issue means "a substance separated from a crude mixture of reactants and/or solvents." The milligram terms have their ordinary meaning, which allows for rounding to the nearest whole number. "About" in the milligram claims at issue has its ordinary meaning of "approximately."

A second phase of claim construction will be needed to complete the construction of two disputed terms. The parties must further brief the question of the ordinary meaning of Term 4, "limited." The parties shall consult and propose a briefing schedule for supplementary briefing on this question. Also, Defendant shall submit a supplementary brief which proposes a particular construction of the ordinary meaning of "C_{max} which results in euphoria." This Court will complete the claim construction of those two terms after supplementary briefing has been completed.

SO ORDERED.

s/ Stanley R. Chesler
STANLEY R. CHESLER, U.S.D.J.

Dated: March 3, 2022